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4. (Amended) The method of claims 1-3, wherein the *hedgehog* therapeutic is a polypeptide which includes a hedgehog amino acid sequence which is identical or homologous to an amino acid sequence of any one of SEQ ID Nos. 10-18.

5. The method of claim 4, wherein the hedgehog amino acid sequence is sufficient for specific binding of the polypeptide to a *patched* protein.

6. The method of claim 4, wherein the hedgehog amino acid sequence is at least 80 percent identical to an amino acid sequence of any one of SEQ ID Nos. 10-18.

7. The method of claim 4, wherein the hedgehog amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions to any one of SEQ ID Nos. 1-9.

8. The method of claim 4, wherein the hedgehog amino acid sequence is of a vertebrate hedgehog protein.

9. The method of claim 4, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate hedgehog protein.

10. The method of claim 4, wherein the polypeptide includes at least an extracellular portion of a vertebrate hedgehog protein corresponding to residues 24-194 of SEQ ID No:15.

11. The method of claim 4, wherein the hedgehog polypeptide is modified with one or more lipophilic moieties.

12. The method of claim 11, wherein the hedgehog polypeptide is modified with one or more sterol moieties.

13. The method of claim 12, wherein the sterol moiety is cholesterol.

14. The method of claim 11, wherein the hedgehog polypeptide is modified with one or more fatty acid moieties.

15. The method of claim 14, wherein each fatty acid moiety is independently selected from the group consisting of myristoyl, palmitoyl, stearoyl, and arachidoyl.

16. The method of claim 11, wherein the hedgehog polypeptide is modified with one or more aromatic hydrocarbons.

17. (Amended) The method of claim 16, wherein each aromatic hydrocarbon is independently selected from benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, and naphthacene.

18. The method of claim 11, wherein the hedgehog polypeptide is modified one or more times with a C7 - C30 alkyl or cycloalkyl.

19. The method of claim 1, wherein the *ptc* therapeutic is a small organic molecule.

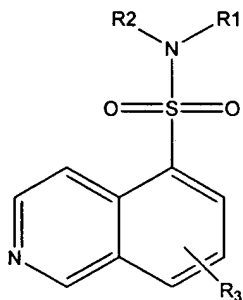
20. The method of claim 19, wherein the binding of the *ptc* therapeutic to *patched* results in up- or down-regulation of *patched* and/or *gli* expression.

21. The method of claim 1, wherein the *ptc* therapeutic binds to *patched* and mimics *hedgehog*-mediated *patched* signal transduction.

22. The method of claim 19, wherein the *ptc* therapeutic is an inhibitor of protein kinase A.

23. The method of claim 22, wherein the PKA inhibitor is a 5-isoquinolinesulfonamide

24. The method of claim 22, wherein the PKA inhibitor is represented in the general formula:



wherein,

R1 and R2 each can independently represent hydrogen, and as valence and stability permit a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a

thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido,  $-(CH_2)_m-R8$ ,  $-(CH_2)_m-OH$ ,  $-(CH_2)_m-O$ -lower alkyl,  $-(CH_2)_m-O$ -lower alkenyl,  $-(CH_2)_n-O-(CH_2)_m-R8$ ,  $-(CH_2)_m-SH$ ,  $-(CH_2)_m-S$ -lower alkyl,  $-(CH_2)_m-S$ -lower alkenyl,  $-(CH_2)_n-S-(CH_2)_m-R8$ , or

R1 and R2 taken together with N form a heterocycle (substituted or unsubstituted);


R3 is absent or represents one or more substitutions to the isoquinoline ring such as a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido,  $-(CH_2)_m-R8$ ,  $-(CH_2)_m-OH$ ,  $-(CH_2)_m-O$ -lower alkyl,  $-(CH_2)_m-O$ -lower alkenyl,  $-(CH_2)_n-O-(CH_2)_m-R8$ ,  $-(CH_2)_m-SH$ ,  $-(CH_2)_m-S$ -lower alkyl,  $-(CH_2)_m-S$ -lower alkenyl,  $-(CH_2)_n-S-(CH_2)_m-R8$ ;

R8 represents a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle; and

n and m are independently for each occurrence zero or an integer in the range of 1 to 6.

25. The method of claim 22, wherein the PKA inhibitor is cyclic AMP analog.
26. The method of claim 22, wherein the PKA inhibitor is selected from the group consisting of N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide, 1-(5-isoquinoline-sulfonyl)-2-methylpiperazine, KT5720, 8-bromo-cAMP, dibutyryl-cAMP and PKA Heat Stable Inhibitor isoform  $\alpha$ .
27. A therapeutic preparation of a small molecule antagonist of *patched*, which *patched* antagonist is provided in a pharmaceutically acceptable carrier and in an amount sufficient to modulate the immune system of an adult human patient.
28. A method for modulating T lymphocytes maturation, comprising administering to a patient a gene activation construct which recombines with a genomic *hedgehog* gene of

the patient to provide a heterologous transcriptional regulatory sequence operatively linked to a coding sequence of the *hedgehog* gene.

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29. A method of claim 2, wherein suppressing the immune function of an animal comprises inhibiting T lymphocyte maturation.
30. A method of claim 3, wherein enhancing the immune function of an animal comprises stimulating T lymphocyte maturation.

*The claims presented above incorporate changes as indicated by the marked-up versions below.*

2. (Amended) A method for suppressing the immune system of an animal comprising [contacting the cells with ]administering to the animal an effective amount of a *hedgehog* protein, or agonist thereof.
3. (Amended) A method for enhancing the immune system of an animal comprising administering to the animal an immunostimulatory amount of a *hedgehog* antagonist.
4. (Amended) The method of any of claims 1-3, wherein the *hedgehog* therapeutic is a polypeptide which includes a hedgehog amino acid sequence which is identical or homologous to an amino acid sequence of any one of SEQ ID Nos. 10-18.
17. (Amended) The method of claim 16, wherein each aromatic hydrocarbon is [o]independently selected from [the group consisting of ]benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, and naphthacene.